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A SAFETY ASSESSMENT OF INGREDIENTS ADDED TO TOBACCO IN THE MANUFACTURE OF CIGARETTES

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I. INTRODUCTION

Flavoring ingredients have traditionally been added to tobacco, and tobacco used in cigarettes commercially manufactured in the United States has always contained such ingredients. Ingredients added to tobacco in the manufacture of cigarettes consist of 3 general types:

Processing aids are used to reduce "tar" and nicotine yields to meet consumer demands and to facilitate the manufacturing process. Most processing aids are recovered during manufacturing, although minute residues of a few parts per million (ppm) range may remain in the tobacco.

Casing Materials and Humectants are added to replace sugars lost during curing of the tobacco, to retain moisture, as a carrier for flavor, and to make the smoke smoother and milder. All casings and humectants used by United States cigarette manufacturers are foods, food products, or ingredients permitted for use in food by the Food and Drug Administration (FDA).

Flavorings are added to tobacco to impart distinctive flavors, and to fortify natural flavors lost during curing and processing of tobacco. They consist of natural herbs and spices, or their essential oils, as well as synthetic flavors. Most flavorings occur at very low levels (i.e. < 1 ppm), usually as part of specific proprietary formulations.

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II. THE EVALUATION OF INGREDIENTS ADDED TO CIGARETTE TOBACCO

The authors of this report, whose qualifications are summarized in the appendix, each independently reviewed the scientific data on ingredients added to cigarette tobacco by the six major United States manufacturers. This report represents their consensus on the safety of the ingredients.

The material examined was extensive, and included the confidential list of the ingredients added to tobacco in the manufacture of cigarettes. The authors were also provided with summary data of all relevant published and unpublished toxicity tests and reports, as well as the original publications of data when requested. Pyrolysis and transfer rate data, maximum use levels, and annual poundage data for the ingredients were also evaluated. Each scientist independently visited the individual tobacco companies to examine the testing and research programs used for the ingredients. Reports and raw data from the studies were made available and were examined as necessary, and each scientist formed an independent opinion regarding the adequacy of the testing and safety of each ingredient.

III. TOXICITY DATA ON INGREDIENTS ADDED TO CIGARETTE TOBACCO

Approximately 98% of all ingredients added to cigarette tobacco in the United States are approved as food additives by the FDA, or have been given the status "Generally Recognized As Safe" (GRAS) by the FDA or other expert committees. Some ingredients are highly volatile and are, thus, lost during the manufacturing process rather than being present in the finished cigarette. Moreover, many of the ingredients are identical or

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essentially similar in composition to natural leaf tobacco components. The pyrolysis products of such ingredients are not expected to depart significantly from the amounts or types of components generated from a range of additive-free tobaccos or tobacco blends. Furthermore, the ingredients do not contribute measurably to tar yields.

The 28 ingredients added to tobacco that are present at the highest levels in cigarettes occur at levels ranging from 0.05% to 9.28% by weight, the latter being sugars. These ingredients, along with the processing aids, also account for more than 99% of the total weight of the ingredients added to cigarette tobacco. All of the remaining ingredients added to tobacco that are present in cigarettes occur at levels below 500 ppm (0.05%), and over one-third occur at levels below 1 ppm (0.0001%).

The authors reviewed extensive data on the ingredients added to cigarette tobacco from large numbers of published and unpublished studies. Included among these data were findings from in vitro and in vivo tests on metabolism, genotoxicity and reproduction, as well as acute, subchronic, and chronic toxicity tests. These studies are of the same type as those used to assess the biological effects of food additives, drugs and environmental chemicals. The objectives of these studies are to determine the exposure levels at which adverse effects may occur and the nature of the adverse effects.

Metabolism studies specifically examine the manner in which a substance is absorbed in the body, broken down, and eliminated. These processes can all be influenced by the doses administered, and they also may vary among species. Such information is.

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therefore, often essential for determining the relevance of high dose effects in animals to the relatively low levels of human exposure.

Genotoxicity studies assess the capacity of a chemical to alter the genetic material in cells. Tests are conducted to detect the potential for inducing either gene mutations, chromosome damage, or DNA damage. Substances which experts recognize as clearly positive in such tests may be harmful, particularly with regard to potential risks of cancer or birth defects.

Acute, subchronic and chronic toxicity studies involve the administration of test substances to animals by routes similar or analogous to those known for humans, at various doses, and for time periods ranging from very brief to lifetime exposures. Animal studies with the ingredients added to cigarette tobacco have included skin painting, inhalation, and oral routes of exposure. The objectives of such studies are to identify the type(s) of toxicity and the organs affected at high test doses, to determine levels of exposure that will pose no unacceptable risks to humans and, in the case of skin painting, to determine tumor promotion effects. These studies require thorough clinical and pathologic evaluations of many test animals during and following the exposures, plus a final interpretation of the relevance of the findings to human risk.

Reproductive studies are specialized types of subchronic and chronic toxicity experiments which specifically examine the effects of a test substance on fertility, gestation, and fetal and neonatal development.

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In reviewing the data related to the safety of ingredients added to cigarette tobacco, emphasis was given to the major ingredients (those comprising 99% of the ingredients added), since exposure to these would be expected to be highest. Most ingredients are present at very low levels as components of proprietary flavor formulations, and exposure, if any, would be toxicologically insignificant. Exposure to many of these flavor ingredients is, in fact, greater through the diet than it is through cigarette smoking.

Although all types of toxicological data have some utility for evaluating the safety of ingredients added to cigarette tobacco, particularly relevant are inhalation studies involving actual smoking experiments in animals which compare the biological effects of inhaling tobacco smoke with and without added ingredients. In such experiments, animals inhale smoke from burning cigarettes for extended periods, and toxicological effects are assessed by thorough clinical and pathologic examinations. Although all body systems are examined, emphasis is given to the upper and lower respiratory tracts and the cardiovascular system. Ingredients added to cigarette tobacco have not been observed to induce adverse effects in these experiments. In fact, in many cases added ingredients have reduced the levels of irritation from tobacco smoke.

The authors also reviewed the available data on pyrolysis of the ingredients added to cigarette tobacco. Based upon such data from representative ingredients, it has been determined that most volatile ingredients do not pyrolyze in burning cigarettes, i.e., they do not decompose or chemically change as a result of heat. They are transferred intact in smoke. Thus, if there is exposure and absorption, metabolism would be similar to

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ingestion. Among those that do pyrolyze, their chemical similarities to tobacco leaf components, and their relatively low levels, suggest that they do not significantly alter the composition of tobacco smoke. In any event, toxicity from pyrolysis products would be evident in smoking studies and, as indicated above, such studies have been negative.

Based upon analyses of all of the toxicological data reviewed by the authors of this report, it was concluded that there was no evidence that any ingredient added to cigarette tobacco produces harmful effects under the conditions of use in cigarettes.

IV. SUMMARY AND CONCLUSION

Ingredients are added to tobacco to aid in processing, retain moisture, add flavor, and reduce "tar" and nicotine yields. They have always been used in commercially manufactured cigarettes in the United States. Most are present at extremely low levels. Among those that pyrolyze, the pyrolysis products are not expected to depart significantly from those of additive-free tobacco.

It is important to recognize that the use of these ingredients has enabled manufacturers to develop cigarettes with lower "tar" and nicotine yields than would otherwise be available, and the primary issue in safety assessment is whether or not cigarettes are potentially hazardous as a result of the added ingredients. A careful analysis of the scientific data clearly indicates that this is not the case.

The 28 ingredients added to tobacco that are present at the highest levels in cigarettes occur at levels ranging from 0.05% to 9.28% by weight. These ingredients, along with processing aids, comprise 99% of the total poundage of ingredients added to

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tobacco in the manufacture of cigarettes, and have been extensively tested for safety. All remaining ingredients occur at lower levels, with many below 0.0001% (1 ppm). Approximately 98% of all ingredients are approved as food additives, or are generally recognized as safe (GRAS) by expert committees, and exposure to these ingredients is generally higher in food than through smoking.

The authors of this report independently examined extensive published and unpublished toxicologic, metabolic, and pyrolysis data on the ingredients added to cigarette tobacco, and found none to be potentially toxic at levels of use.

It is concluded that the ingredients added to tobacco in the manufacture of cigarettes by the six major United States manufacturers are not hazardous under the conditions of use.

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